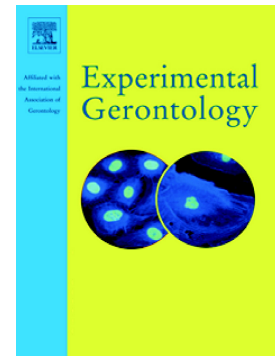


Accepted Manuscript

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PII: S0531-5565(16)30296-0
DOI: doi: [10.1016/j.exger.2017.03.003](https://doi.org/10.1016/j.exger.2017.03.003)
Reference: EXG 10015

To appear in: *Experimental Gerontology*

Received date: 30 August 2016
Revised date: 24 February 2017
Accepted date: 2 March 2017

Please cite this article as: Brendon Stubbs, Li-Jung Chen, Chun-Yi Chang, Wen-Jung Sun, Po-Wen Ku , Accelerometer-assessed light physical activity is protective of future cognitive ability: A longitudinal study among community dwelling older adults. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Exg(2017), doi: [10.1016/j.exger.2017.03.003](https://doi.org/10.1016/j.exger.2017.03.003)

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Accelerometer-assessed light physical activity is protective of future cognitive ability:**A longitudinal study among community dwelling older adults**

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Running title: Accelerometer-assessed light physical Activity and cognitive impairment

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Abstract

Objective (246/250)

Physical activity (PA), especially moderate-to-vigorous intensity, could protect older adults from cognitive impairment. However, most literature is based on self-reported PA which is limited by recall bias. Light PA is popular among older adults, but a paucity of objective longitudinal data has considered the relationship between light PA and cognitive ability. We examined if a higher level of objectively measured light PA, independent of moderate-to-vigorous physical activity (MVPA), was prospectively associated with better cognitive ability in older adults.

Methods

A longitudinal study over 22.12 (± 1.46) months including 274 community-dwelling older adults across 14 regions in Taiwan was undertaken. Cognitive ability was obtained using a Chinese version of the Ascertain Dementia 8-item Questionnaire (AD8) and light PA and MVPA captured by 7 days accelerometer positioned on waist. Multivariable negative binomial regression adjusted for confounders were undertaken.

Results

274 participants (74.52 years, 45.6% male) attended the follow-up (96.1%). Higher light PA, independent from MVPA, was associated with a reduced rate of decline in cognitive ability (rate ratio 0.75 [0.60-0.92]). MVPA, was also associated with a reduced decline in cognitive ability (rate ratio 0.85 [0.75-0.95]). Light PA was protective of cognitive ability in sensitivity analyses removing participants with activities of daily living difficulties, depressive symptoms and cognitive impairment at baseline.

Conclusion

Our data suggest that light PA may offer a protective influence of future cognitive ability in community dwelling older adults. The promotion of light PA may be a valuable means to maintain cognitive ability in older age.

Key words: Cognitive decline, dementia, light physical activity, moderate to vigorous physical activity, older adults, old age, cognition

Introduction

Dementia is a common neurodegenerative condition among older adults that typically leads to a loss of independence, reduced quality of life, premature mortality, caregiver burden and high levels of healthcare utilization and cost (Fiest et al. 2016; Prince et al. 2013). Given the aging population, the total number of dementia cases will inevitably increase, and there are pressing calls to prevent cognitive decline and ultimately dementia (Deckers et al. 2015).

Within the last twenty years there has been a rapid increase in interest for the potential of physical activity to prevent cognitive decline and maintain good cognitive ability (Barnes and Yaffe 2011; Deckers et al. 2015; Hamer and Chida 2009). Two recent systematic reviews stipulated that physical activity is one of the top seven modifiable risk factors for cognitive impairment in older age (Barnes and Yaffe 2011; Deckers et al. 2015). A recent meta-analysis of longitudinal studies found that higher baseline levels of physical activity were associated with a 14% reduced risk of future dementia (Relative risk (RR) 0.86, 95% CI 0.76-0.97) (Blondell et al. 2014). The authors (Blondell et al. 2014) only identified one study capturing physical activity utilizing an objective measurement of physical activity (Buchman et al. 2012), which found that higher total physical activity was independently associated with a reduced risk of Alzheimer's disease over 4 years.

Capturing physical activity with self-report measures among older adults, even in the absence

of altered cognitive ability or cognitive impairment, is challenging. In fact, a recent systematic review of psychometric and measurement properties of self-report physical activity measures in older adults noted that most self-report measures have little evidence of any validity and reliability (Falck et al. 2016). Whilst a small number of cross sectional studies have investigated objective physical activity and cognition in older age (Doi et al. 2015; Makizako et al. 2015), there remains a paucity of longitudinal studies investigating objectively measured physical activity and cognitive impairment/ability. Another key limitation in the literature is that international physical activity guidelines recommend that older adults should do at least 150 minutes of moderate-intensity aerobic physical activity or do at least 75 minutes of vigorous intensity aerobic physical activity throughout the week. This appears to imply that little or no health benefits can be derived from light physical activities (World Health Organization 2010). Light physical activity is a popular, relatively safe and effective form of activity for older adults (Tse et al. 2015). Physical activity conducted at moderate to vigorous intensity, whilst conferring potentially greater benefits may also carry a greater risk of injury and potential dropout from exercise (Tse et al. 2015). Thus, understanding if light intensity physical activity (e.g. casual walking, stretching, and light yard/house work etc.), independent of moderate-to-vigorous physical activity (MVPA), might offer protective effects on cognitive ability could provide clinically useful information. Given the paucity of longitudinal studies considering the relationship between light intensity

physical activity and cognitive abilities using objective devices, the current study examined whether objectively measured light physical activity, independent of MVPA, is associated with a reduced risk of decline in cognitive ability in older adults. To test for confounding and reverse causation, sensitivity analyses were also conducted.

Methods

Study design and sample

The current longitudinal study utilized data from two-waves of a community-based project conducted in Hunei District, Kaohsiung, which is the second largest city in Taiwan. In total, 285 community-dwelling older adults who were aged 65 years or older were recruited and assessed from August to October 2012. Participants were recruited from 14 village regions, with approximately 20 people being recruited from each community center utilizing quota sampling in which, participants were drawn based on a national distribution according to sex and age in 2011 (Taiwan Ministry of Interior 2012). Follow up interviews were conducted between May to July 2014. From the baseline sample, 274 participants (96.1%) attended the follow-up after a mean of 22.12 ± 1.46 months. The reasons why participants ($n=11$) did not attend the assessment of the second wave included: Inpatient ($n=2$), not traceable ($n=2$), deceased cases ($n=4$) and refuse to attend ($n=3$).

All participants provided written consent at the time of enrollment. This study obtained

ethical approval from National Taiwan University of Sport Institutional Review Board, Taiwan. All data was collected using a standardized interview format, conducted with face-to-face interviews at each person's house.

Measures

Cognitive ability

Cognitive ability was obtained using a Chinese version of the Ascertain Dementia 8-item Questionnaire (AD8) by participants with a potential range between 0 and 8 (Galvin et al. 2005; Galvin et al. 2007). The AD8 comprises 8 items that ask the respondents to rate change in memory, problem-solving abilities, orientation, and daily activities (yes=1, no=0). Higher scores represent cognitive ability decline (Galvin et al. 2005; Ganguli et al. 2014). The Chinese version of the AD8 has demonstrated adequate reliability and validity among community-dwelling older Taiwanese adults (Yang et al. 2011). Within the current study, the Cronbach's alpha reliability coefficients for the AD8 ranged between 0.79 (first-wave) and 0.81 (second-wave) across the two waves of data collection.

Objective physical activity

Physical activity were captured using waist worn triaxial accelerometer monitors (GT3X+, ActiGraph, Pensacola, FL, USA) for 7 days. In order to be included in the study, participants had to wear the accelerometer for a minimum of 10 hours of monitoring on at least 5 days (Buman et al. 2010). Data were processed and scored using the ActiLife 6.2

software (ActiGraph, Pensacola, FL, USA). Periods of 60 min of consecutive zero counts were considered as non-wearing time and were excluded from the analyses. Physical activity parameters were then computed using established cut offs, comprising time spent in light physical activity (100–1951 counts/min), and moderate-to-vigorous activity (>1951 counts/min) (Gorman et al. 2014), together with total physical activity energy expenditure (kcal/week). Research evidence has demonstrated that there is a strong correlation between the indirect calorimetry estimates of energy expenditure and energy expenditure (kcal) assessed by GT3X+ ($r = 0.82$) (McMinn et al. 2013). For descriptive purposes, the various physical activity categories were converted into tertiles, but the primary analyses were conducted on continuously distributed variables.

Covariates

A number of covariates were collected at baseline in line with previous literature (Coley et al. 2008; Hamer and Chida 2009): including (i) socio-demographic factors: sex, age (65–74 years, 75+ years), educational attainment (no formal schooling, primary school, secondary school+), marital status (married/cohabitating, others), main source of income (from offspring vs. self [e.g. pension/savings]); (ii) lifestyle behaviors: smoking status (current, never, or former smokers), alcohol consumption (yes vs. no), and; (iii) health status: body mass index (BMI) (<18.50, 18.50–23.99, 24–26.99, 27+), (Taiwan Department of Health 2003) number of chronic diseases (0, 1, 2+), which included hypertension, stroke, diabetes, heart disease,

cancer, chronic obstructive pulmonary disease (COPD), liver disease, renal disease, and arthritis; difficulties with activities of daily living (ADLs, no difficulties at all vs. some or great difficulties); depressive symptoms assessed by the 15-item Geriatric Depression Scale (GDS) using cutoff of 5 (no vs. yes), (Brink et al. 1982; Yesavage and Sheikh 1986); mean daily accelerometer wear time (Hamer et al. 2014), and baseline AD8 scores.

Data analysis

Descriptive statistics were used to describe the features of the study sample. Given the violation of normality, Mann Whitney U tests and Kruskal-Wallis tests were adopted to check for differences in cognitive ability in 2014 across levels of accelerometer-derived parameters (all in tertiles), and covariates. Previous research indicated that the use of the conventional level (p -value = 0.05) may fail to identify variables known to be important. Variables with a p value less than 0.25 were included in the subsequent regression models for adjustment (Hosmer et al. 2013).

To examine the bi-correlations between objectively assessed physical activity parameters and subsequent cognitive ability after controlling for accelerometer wear time, partial correlation coefficients between physical activity energy expenditure (kcal/week as a continuous variable), time (hours/day as a continuous variable) spent in physical activity at light and moderate-to-vigorous intensities, and subsequent cognitive ability were computed.

Multivariable negative binomial regression was conducted because the outcome variable was an over-dispersed count with a highly skewed distribution. All accelerometer-derived physical activity parameters were log-transformed before conducting regression analyses due to non-normality (Tudor-Locke et al. 2011). Two separate unadjusted regression models (single-factor models) for light and moderate-to-vigorous activity were conducted to assess the associations between each intensity categories and cognitive ability. Then, two separate multivariable regression models (single-factor models) for light and moderate-to-vigorous activity (without mutual adjustment) were conducted to assess the associations between each intensity categories and cognitive ability after adjusting for baseline cognitive ability, wear time of accelerometer, socio-demographic variables, lifestyle behaviors, and chronic conditions. Finally, one multivariable regression model (a two-factor model) for light activity was fitted to examine the relationships in more detail after adjusting for MVPA and other covariates.

Sensitivity analyses were carried out to evaluate confounding and reverse causation. In first stage, we considered the possibility that ADL difficulties might influence physical activity behaviors at baseline and subsequent cognitive ability, so the negative binomial regressions were repeated after excluding the 13 participants with impaired ADLs. At the second stage, we mitigated the potential impact of depressive symptoms on physical activity and cognitive ability at baseline by excluding participants with depressive symptoms (n= 49)

(Guo et al. 1988). At the third stage, participants with suspected mild cognitive ability or dementia (i.e. AD8 scores equal or greater than 2) at baseline (n=65) which may have been not only associated with baseline physical inactivity and subsequent health conditions but also associated with the accuracy of survey responses. Sensitivity analysis was conducted excluding those with suspected mild cognitive impairment or dementia at baseline.

All analyses were conducted using IBM SPSS 20.0 software and a p value < 0.05 was considered statistically significant.

Results

Full details of the sample with follow up data are presented alongside AD8 cognition scores in Table 1. At baseline, the mean score of AD8 was 0.80 (SD= 0.93). The mean age of the sample was 74.52 (SD= 6.12) years, just under half of the sample were male (45.6%), while the majority of the sample did not smoke (86.8% nonsmokers) or drink alcohol (95.2% non-drinkers). In the univariate analyses, higher AD8 scores at follow-up (i.e. worse cognition) were associated with female gender, increasing age, lower education status, low light PA, MVPA, total physical activity, more chronic conditions, and having depressive symptoms and ADL difficulty at baseline (see Table 1).

Table 1 Distribution of cognitive ability in 2014 between levels of descriptors in 2012

Variables in 2012	N	AD8 scores in 2014 Mean (SD)	<i>p</i> -value ^a
Socio-demographic			
Sex			0.003
Male	125	0.85 (1.31)	
Female	149	1.29 (1.61)	
Age			0.001
65-74	156	0.81 (1.22)	
75+	118	1.45 (1.74)	
Education level			0.002
Secondary school+	48	0.46 (0.46)	
Primary school	113	1.17 (1.17)	
No formal schooling	113	1.27 (1.27)	
Marital status			0.002
Married	192	0.92 (0.93)	
Others	82	1.48 (1.48)	
Main source of income			0.001
Offspring	139	0.83(1.34)	
Self (pension/savings)	135	1.35(1.61)	
Lifestyle behaviors			
Total energy expenditures (kcal/wk)			< 0.001
High	92	0.48(0.75)	
Medium	91	0.90 (1.27)	
Low	91	1.89 (1.89)	
Moderate-to-vigorous PA (hour/day)			< 0.001
High	92	0.55 (0.75)	
Medium	88	1.08 (1.51)	
Low	94	1.62 (1.83)	
Light PA (hour/day)			<0.001
High	93	0.54 (0.67)	
Medium	91	1.04 (1.61)	
Low	90	1.70 (1.76)	
Smoking			0.122
Never smoker	238	1.03 (1.46)	
Current smoker	22	1.36 (1.65)	
Former smoker	14	1.71 (1.77)	

Alcohol consumption				0.696
No	261	1.08 (1.49)		
Yes	13	1.31 (1.75)		
Health Status				
Body mass index				0.888
Underweight <18.5	11	1.18 (1.78)		
Normal 18.5-23.99	101	1.06 (1.26)		
Overweight 24-26.99	101	1.12 (1.70)		
Obese 27+	61	1.07 (1.47)		
Number of chronic diseases				0.041
0	118	0.86 (1.30)		
1	104	1.13 (1.37)		
2+	52	1.52 (2.00)		
Depressive symptoms				0.018
No	225	0.99 (1.41)		
Yes	49	1.53 (1.78)		
Activities of daily living				0.012
No difficulty at all	261	1.03 (1.44)		
Some or great difficulties	13	2.23 (2.13)		
Baseline cognitive ability (AD8)	274	$\rho = 0.455^b$		$< 0.001^b$

AD8= The Ascertain Dementia 8-item Informant Questionnaire (AD8)

a: Mann Whitney U test or Kruskal-Wallis test

b: Spearman correlation

Correlation analyses between physical activity and subsequent cognitive ability

Table 2 summarizes the partial correlations between each physical activity category at baseline, and subsequent cognitive ability. Briefly, worse cognition was negatively associated with total PA, light and MVPA (data in Table 2).

Table 2 Partial correlation coefficients between baseline physical activity parameters and cognitive ability at follow-up adjusting for mean daily accelerometer wear time (n=274)

Variables (continuous)	Baseline			Follow-up
	Energy expenditures	MVPA	LPA	Cognitive ability
Energy expenditures	1.00			
MVPA	0.75***	1.00		
LPA	0.79***	0.39***	1.00	
Cognitive ability	-0.35***	-0.25***	-0.39***	1.00

MVPA: Moderate-to-vigorous physical activity; LPA: Light physical activity;

*** $p < 0.001$

Multivariate relationship between physical activity and subsequent cognitive score

The crude and adjusted estimates of single and multifactor models are presented in Table 3.

In the crude and adjusted analyses of single-factor models, light physical activity and MVPA were both significantly associated with a reduced rate of cognitive ability decline. In the adjusted estimates of two-factor model, light physical activity was independent from MVPA and associated with a reduced rate of cognitive ability decline with a rate ratio of 0.75 (0.60-0.92). Similarly, MVPA was also independent from light PA and associated with a reduced rate of cognitive ability decline (rate ratio 0.85 (0.75-0.95)).

Table 3 Negative binomial regression models examining the crude and adjusted effects of light physical activity at baseline on subsequent cognitive ability (n=274)

Physical activity (continuous)	Single-factor models				Two-factor model	
	Crude RR (95% CI) ^a	<i>P</i>	Adjusted RR (95% CI) ^b	<i>p</i>	Adjusted RR (95% CI) ^c	<i>p</i>
MVPA	0.74 (0.66-0.82)	< 0.001	0.81 (0.72-0.91)	< 0.001	0.85 (0.75-0.95)	0.006
LPA	0.53 (0.45-0.64)	< 0.001	0.67 (0.53-0.84)	0.001	0.75 (0.60-0.92)	0.007

RR= rate ratio; MVPA= moderate-to-vigorous physical activity; LPA= light physical activity

a: The two (single-factor) regression models for estimating the crude RR represent the unadjusted association of MVPA or LPA with cognitive impairment without mutual adjustment.

b: The two (single-factor) regression models for estimating the adjusted RR represent the multivariable association of MVPA or LPA with cognitive ability without mutual adjustment. Covariates in the two models: baseline cognitive scores, sex, age, educational attainment, marital status, income source, smoking, number of chronic diseases, depressive symptoms, activities of daily living, and wear time of accelerometer

c: The (two-factor) regression model for estimating the adjusted RR represent the multivariable association of LPA with cognitive ability.

Covariates in the model: baseline cognitive scores, sex, age, educational attainment, marital status, income source, smoking, number of ability chronic diseases, depressive symptoms, activities of daily living, wear time of accelerometer, and MVPA,

Sensitivity analyses

The crude and adjusted analyses of single and multifactor models in sensitivity analyses are shown in Table 4. To examine confounding and reverse causation, sensitivity analyses were conducted to exclude people with ADL difficulty, people with both ADL difficulty and depressive symptoms, and those with suspected cognitive impairment at baseline respectively. However, the effect of light physical activity on subsequent cognitive ability remained. The patterns of physical activity with cognitive ability at follow-up were similar to those in Table 3.

Table 4 Sensitivity analyses for assessing the robustness of the associations between baseline physical activity parameters and subsequent cognitive ability

Stage 1: Excluding participants with ADL difficulties at baseline (n= 261)						
Physical activity (continuous)	Single-factor models				Two-factor model	
	Crude RR (95% CI) ^a	<i>p</i>	Adjusted RR (95% CI) ^b	<i>p</i>	Adjusted RR (95% CI) ^c	<i>p</i>
MVPA	0.73 (0.65-0.82)	< 0.001	0.81 (0.71-0.92)	0.002	0.85 (0.74-0.97)	0.018
LPA	0.53 (0.44-0.64)	< 0.001	0.68 (0.54-0.86)	0.001	0.74 (0.58-0.95)	0.017
Stage 2: Excluding participants with ADL difficulties and depressive symptoms at baseline (n= 216)						
Physical activity	Crude RR (95% CI) ^a	<i>p</i>	Adjusted RR (95% CI) ^b	<i>p</i>	Adjusted RR (95% CI) ^c	<i>p</i>
MVPA	0.75 (0.67-0.85)	< 0.001	0.81 (0.70-0.94)	0.005	0.86 (0.74-0.99)	0.043
LPA	0.50 (0.39-0.64)	< 0.001	0.62 (0.45-0.84)	0.002	0.69 (0.51-0.94)	0.018
Stage 3: Excluding participants with suspected cognitive impairment at baseline (n=209)						
Physical activity	Crude RR (95% CI) ^a	<i>p</i>	Adjusted RR (95% CI) ^b	<i>p</i>	Adjusted RR (95% CI) ^c	<i>p</i>
MVPA	0.79 (0.69-0.89)	< 0.001	0.79 (0.69-0.93)	0.003	0.86 (0.73-1.00)	0.050

LPA	0.57 (0.45-0.74)	< 0.001	0.60 (0.44-0.81)	0.001	0.69 (0.51-0.95)	0.021
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RR= rate ratio; MVPA= moderate-to-vigorous physical activity; LPA= light physical activity

a: The two (single-factor) regression models for estimating the crude RR represent the unadjusted association of MVPA or LPA with cognitive ability without mutual adjustment.

b: The two (single-factor) regression models for estimating the adjusted RR represent the multivariable association of MVPA or LPA with cognitive ability without mutual adjustment. Covariates in the two models: baseline cognitive scores, sex, age, educational attainment, marital status, income source, smoking, number of chronic diseases, depressive symptoms, activities of daily living, and wear time of accelerometer

c: The (two-factor) regression model for estimating the adjusted RR represent the multivariable association of LPA with cognitive ability. Covariates in the model: baseline cognitive scores, sex, age, educational attainment, marital status, income source, smoking, number of chronic diseases, depressive symptoms, activities of daily living, wear time of accelerometer, and MVPA.

Discussion

The current study established that objective light physical activity offers a protective effect from future decline in cognitive abilities over approximately two years among community dwelling older adults. The protective effects of light physical activity were independent of MVPA and the results remained robust in sensitivity analyses removing those people with difficulties with ADL, depressive symptoms and suspected mild cognitive impairment at baseline.

With the rapidly growing number of older people across the world, our data that objective light physical activity confers a protective effect for future cognitive abilities are welcome and has potential public health implications. Previous reviews (Blondell et al. 2014; Hamer and Chida 2009; Paterson and Warburton 2010) have repeatedly highlighted the absence of studies considering objective physical activity data and future cognitive impairment. Thus, the overwhelming reliance of self-report physical activity from previous studies has infiltrated a bias within the literature and such questionnaires cannot accurately disentangle the potential individual benefits of different intensities of physical activity. The unique protective influences of light physical activity on cognition are welcome for a number of reasons. First, light physical activity such as casual walking, gardening and household chores are a preferred method of accumulating physical activity for older people (Farren et al. 2015). Moreover, light physical activities may also offer opportunities to interactive with neighbors, families

and friends and reduce the risk of social isolation. In addition, light physical activity is associated with better wellbeing, physical health (Buman et al. 2010; Ku et al. 2016) and improvements in other health outcomes such as reducing blood pressure, body fat, cholesterol and improving cardiorespiratory fitness (Hanson and Jones 2015). Moreover, the risk of injury and adverse outcomes are typically less with light physical activity versus more vigorous intensities (Paterson and Warburton 2010). However, there are clearly benefits for engaging in higher intensity physical activity and our data also establish that MVPA has a protective effect on future cognitive impairment. In particular, higher intensity physical activity that improves cardiorespiratory fitness confers particular benefits on health and brain function (Erickson et al. 2014; Erickson et al. 2012).

The potential mechanisms by which physical activity confers a cognitive benefit in older age are yet to be fully disentangled. One potential mechanism is through improving brain structure and grey matter volume and in particular stimulating hippocampal neurogenesis, with more recent evidence also suggesting the caudate nucleus and thalamus may be positively impacted (Erickson et al. 2014; Erickson et al. 2012; Erickson et al. 2011; Kramer and Erickson 2007). There is also accumulating evidence that participating in exercise may improve cognitive outcomes through numerous biomarkers. In particular, recent data suggests that brain-derived neurotrophic factor, cholesterol, testosterone, estradiol,

dehydroepiandrosterone may be associated with improved cognition and reduced dementia risk following exercises in older age (Jensen et al. 2015; Maass et al. 2016). Clearly, future research utilizing objective measures of physical activity are required to disentangle potential mechanistic changes associated with cognitive status in older age.

Whilst our data are novel, one should note the observation nature of the data, which cannot make claims regarding causality. The study follow up time was relatively short. Future longitudinal research of longer duration is required to verify our findings. In addition, future interventional work should seek to establish if changing physical activity levels can improve cognitive (and other) outcomes. Another potential limitation is that objectively assessed physical activity was only measured at baseline, which clearly limits the ability to explore the reciprocal relationships between light physical activity and cognitive ability. Furthermore, there is heterogeneity of comorbid conditions or health status in the population aged 65 or above (e.g., different age groups). Future studies are encouraged to assess the relationships of objectively measured physical activity with cognition, stratified by age groups. In addition, we included some participants at baseline who had some degree of cognitive impairment, which may influence the physical activity status at baseline. However, the independent impact of light physical activity was evident in sensitivity analyses when such participants were removed to mitigate the possibility of reverse causation. Moreover, presenting the data

with and without such participants may actually increase representativeness, given the high numbers of older people who are affected by cognitive impairment. This is the first longitudinal paper to investigate light intensity physical activity and cognitive ability in older adults. Strengths of our paper include the objective measurement of physical activity, adjustment for multiple underlying confounders (e.g. baseline cognitive status, depressive symptoms, and ADL difficulties) known to influence both physical activity and cognitive ability, and test for reverse causation.

In conclusion, our data suggest that engagement in light intensity physical activity, independent of MVPA, is associated with a reduced rate of cognitive ability decline in community dwelling older adults. In addition, objectively assessed MVPA is associated with better cognitive status. This extends the existing evidence for the benefits of physical activity for preventing cognitive decline/impairment in older adults.

Acknowledgements

The authors declare no conflicts of interest and acknowledge funding support from Taiwan Ministry of Science and Technology (104-2410-H-018-028).

Conflict of interest statement

The authors confirm that there are no financial conflicts of interest associated with this paper.

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Highlight Points

- A paucity of studies have considered objective longitudinal physical activity and future cognitive ability decline in older adults.
- Our data suggests that higher light physical activity, independent of moderate-to-vigorous physical activity, is associated with a reduced risk of future cognitive decline.
- This is the first longitudinal paper to investigate light intensity physical activity and cognitive decline in older adults.
- This extends the existing evidence for the benefits of physical activity for preventing cognitive deterioration in later life.